

A Clinical Discussion Of Mixed States In Bipolar Disorder



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Otsuka Pharmaceutical Development &
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Learning Objectives



Review DSM-IV vs DSM-5.0 definitions of “mixed states”

Discuss symptomatology/comorbidity differences between pure and mixed bipolar disorder

Understand relationships between mixed states, substance abuse comorbidity, and suicidality

Consider differential treatment options for patients with mixed vs pure bipolar disorder

DSM, Diagnostic and Statistical Manual of Mental Disorders.

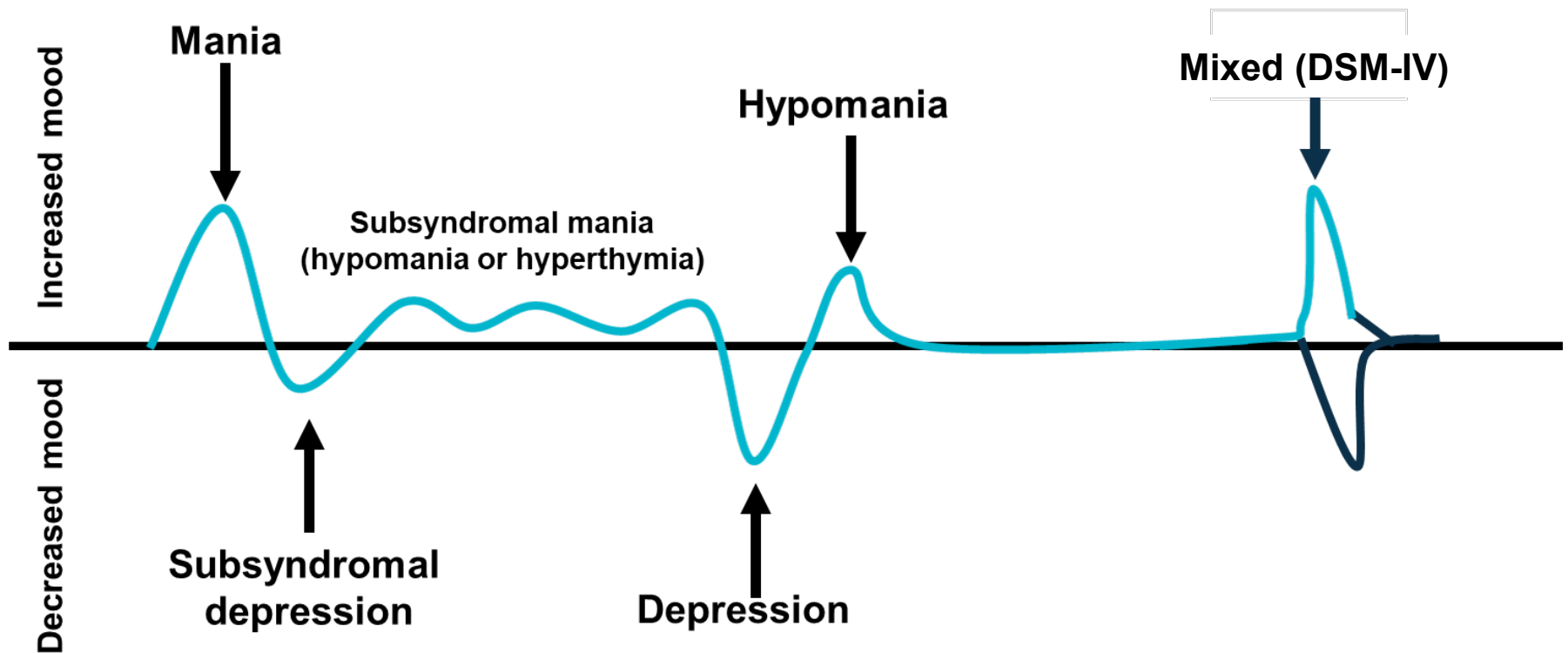
Audience Polling Question

One significant reason for diagnostic delay in bipolar disorder is the possible heterogeneity of clinical presentation. True or False?

A. True

B. False

Mixed BD States Entail Simultaneous Occurrence of Both Manic and Depressive Symptoms¹



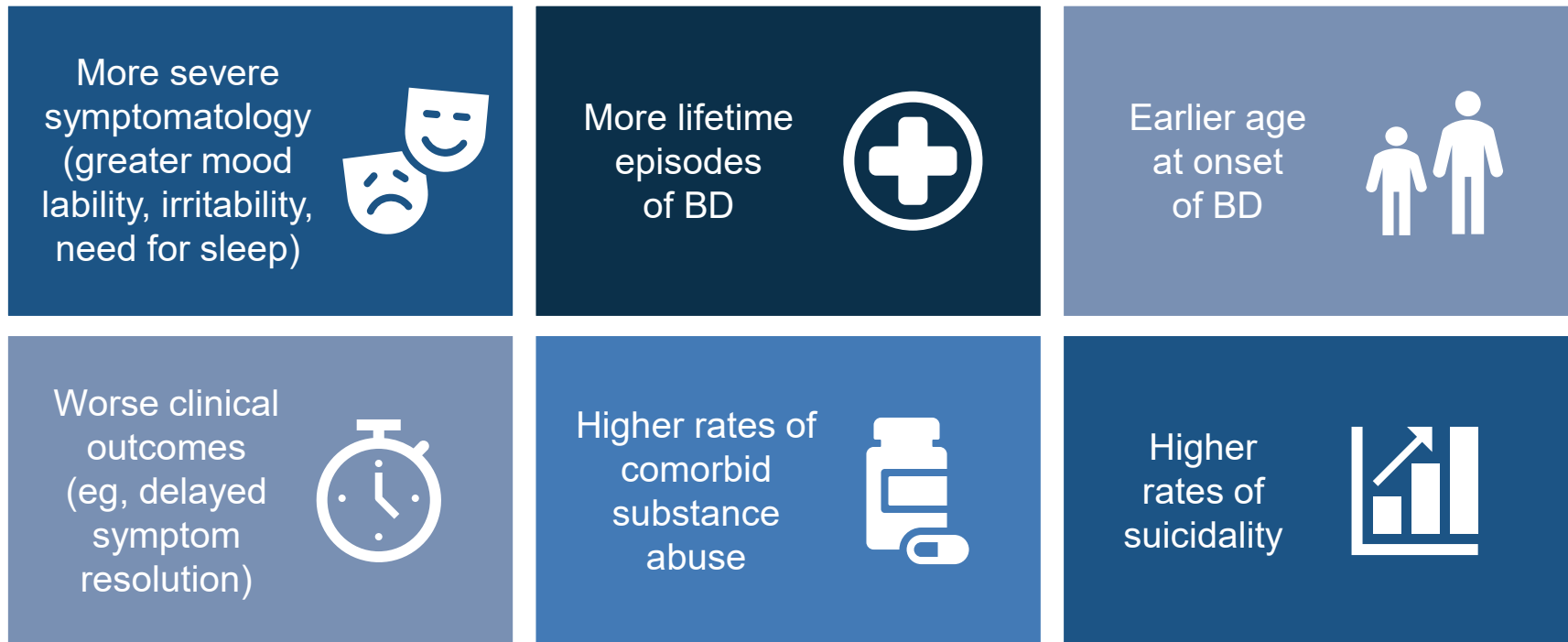
Compared with pure states, mixed BD states may be more challenging to diagnose and treat²

BD, bipolar disorder; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th edition.

1. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. 2013. 2. Fagiolini et al. *CNS Drugs*. 2015;29:725-740.

Mixed Versus Non-Mixed BD Presentations Differ

Compared with patients with BD without mixed features, patients with mixed states generally have

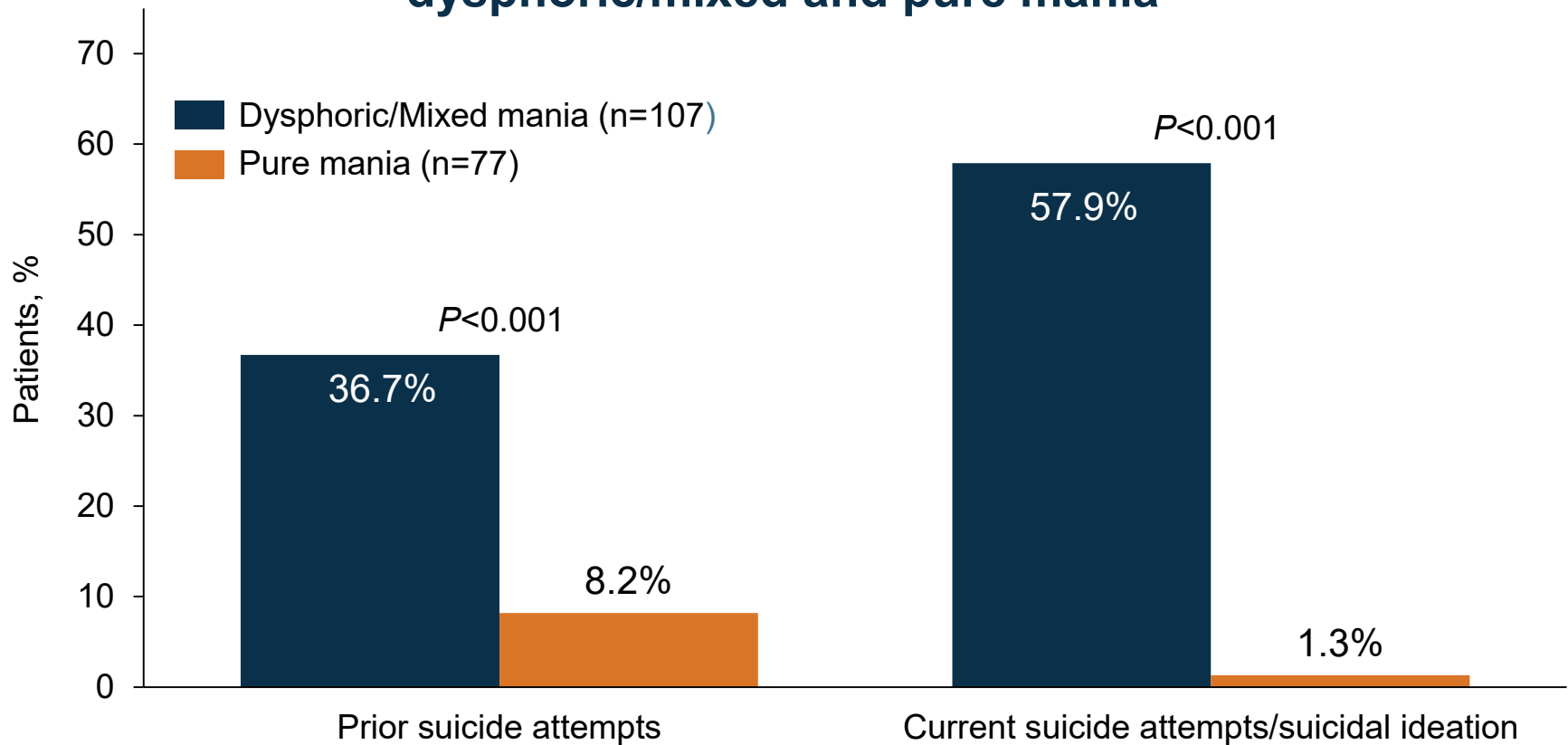


BD, bipolar disorder.

Fagiolini et al. *CNS Drugs*. 2015;29:725-740.

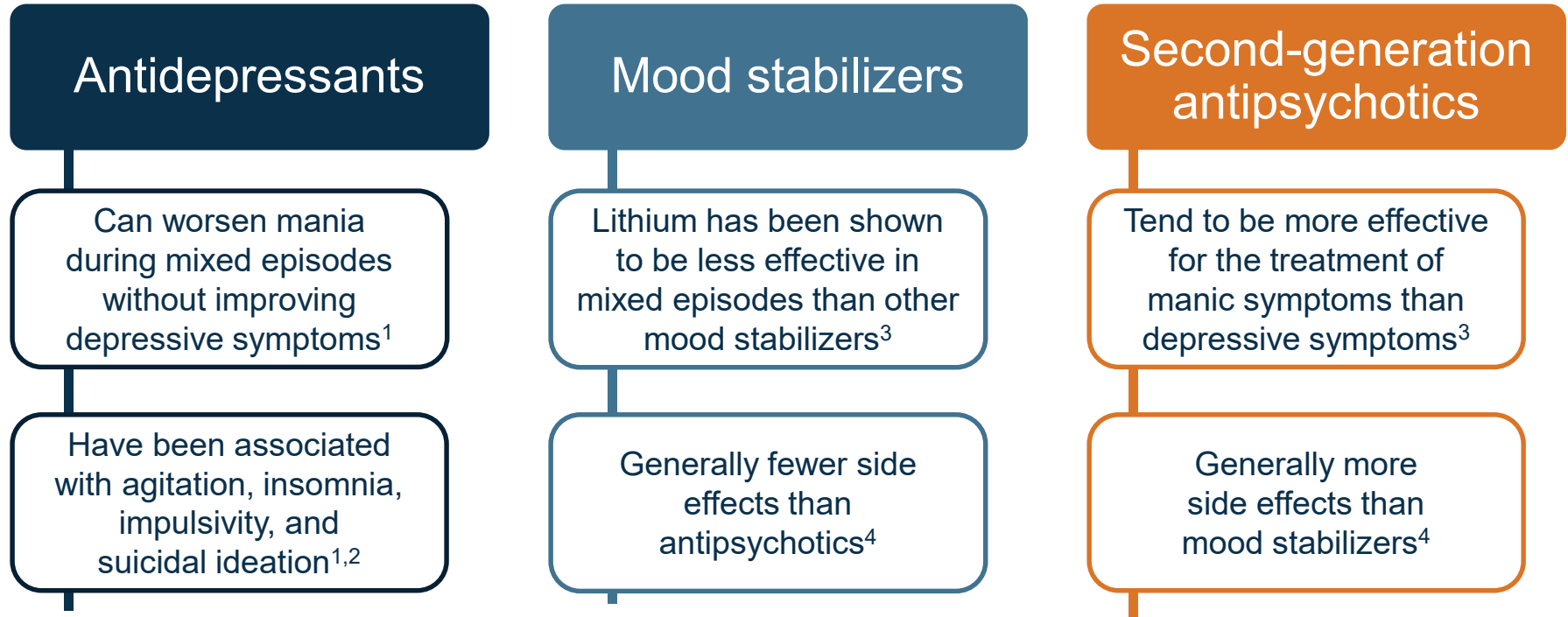
DSM-IV Mixed Mania BD Is Associated With Greater Prior and Current Suicidality

Patients with bipolar disorder (N=184) with lifetime dysphoric/mixed and pure mania



BD, bipolar disorder; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th edition.
Goldberg et al. *Am J Psychiatry*. 1998;155:1753-1755.

Treatment Efficacy Data for DSM-5.0 Mixed States BD Are Limited



BD, bipolar disorder; DSM, Diagnostic and Statistical Manual of Mental Disorders.

1. Pacchiarotti et al. *Am J Psychiatry*. 2013;170:1249-1262. 2. Koukopoulos et al. *Acta Psychiatr Scand Suppl*. 2007;50-57. 3. Fagiolini et al. *CNS Drugs*. 2015;29:725-740. 4. Ketter et al. *J Affect Disord*. 2014;169(suppl 1):S24-S33.

Audience Polling Question

Based on your clinical experience, what percentage of your patients present with DSM-5.0 mixed states?

A. 0% to 10%

B. 11% to 30%

C. 31% to 50%

D. >50%

Audience Polling Question

Based on your clinical experience, what percentage of your patients SHOULD present with DSM-5.1 mixed states?

A. 0% to 10%

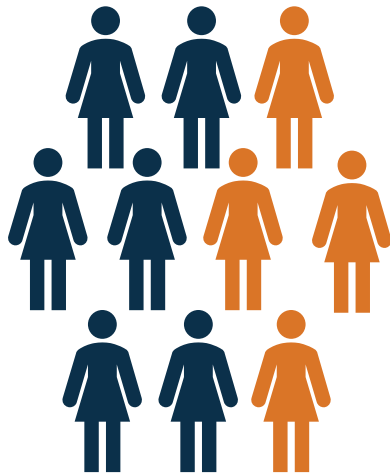
B. 11% to 30%

C. 31% to 50%

D. >50%

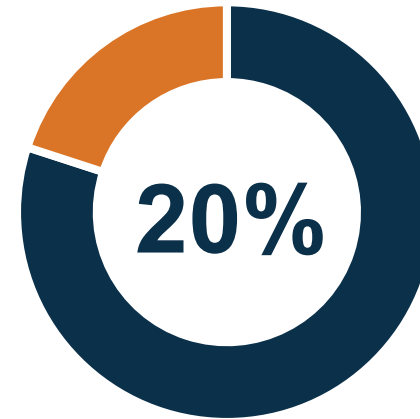
Variable Mixed Feature Prevalence in BD Results in Heterogeneous Symptoms and Challenging Diagnosis

Approximately 40% of patients with BD may experience mixed episodes¹



The prevalence of mixed mania is higher in women than men²

A 2000 DMDA survey of 600 patients with BD reported that only 20% were correctly diagnosed within the first year³

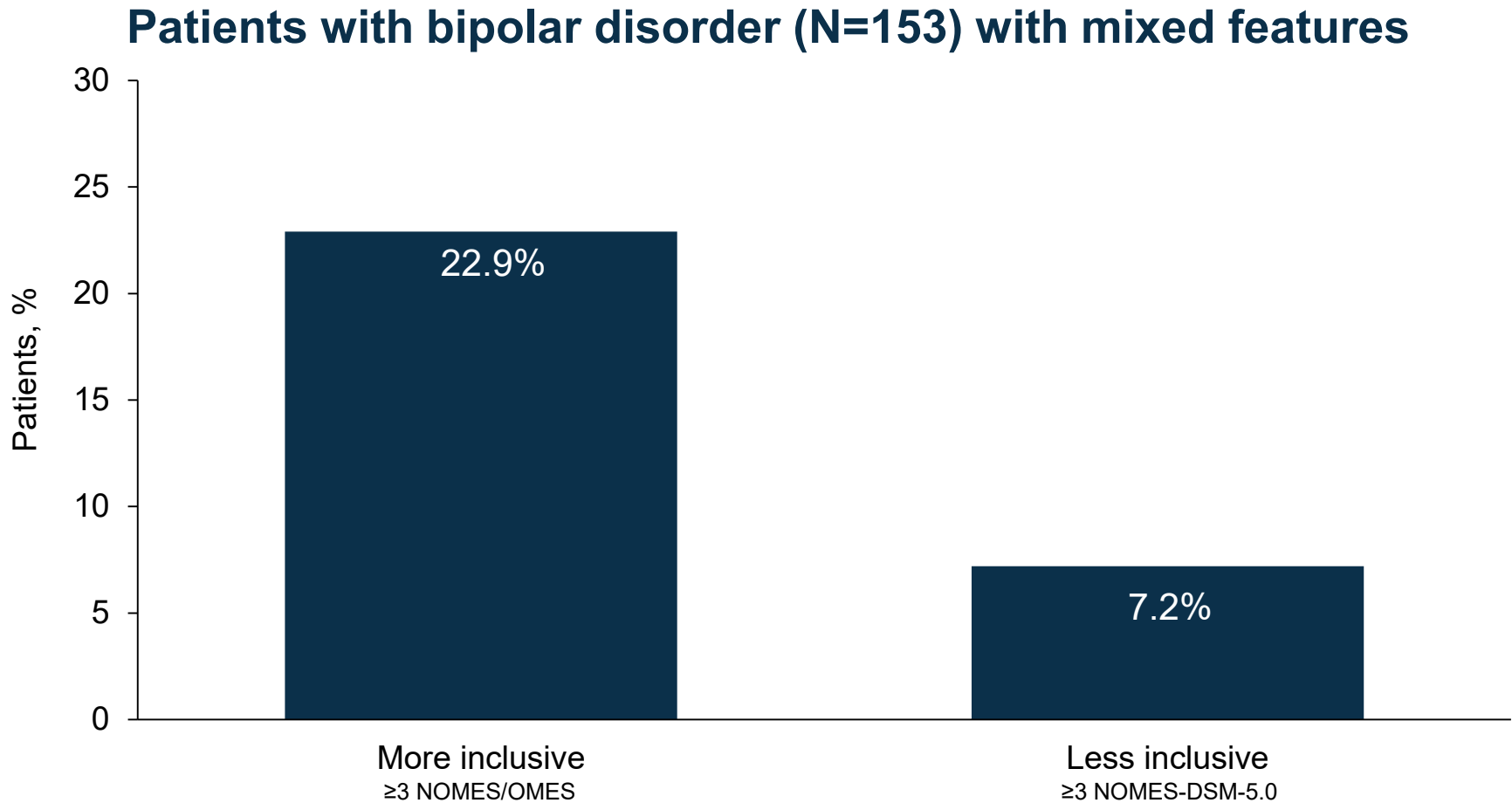


Delay may be due, in part, to the frequency of mixed symptoms, making diagnosis challenging⁴

BD, bipolar disorder; DMDA, National Depressive and Manic-Depressive Association.

1. Fagiolini et al. *CNS Drugs*. 2015;29:725-740. 2. Cassidy et al. *Bipolar Disord*. 2008;10:131-143. 3. Hirschfeld et al. *J Clin Psychiatry*. 2003;64:161-174. 4. Hu et al. *Prim Care Companion CNS Disord*. 2014;16:PCC.13r01599.

Higher Mixed Depression Prevalence Using More Inclusive Versus Less Inclusive Threshold



DSM, Diagnostic and Statistical Manual of Mental Disorders; NOMES, non-overlapping mood elevation symptoms; OMES, overlapping mood elevation symptoms.
Kim et al. *Acta Psychiatr Scand.* 2016;134:199-206.

Audience Polling Question

Based on your clinical experience, which of the following potential mixed states do you believe should count toward DSM-5.1 “with mixed features”?

A. Distractibility

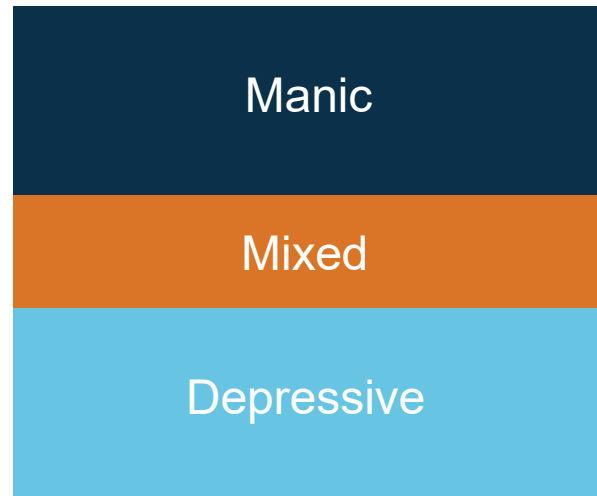
B. Irritability

C. Psychomotor agitation

D. None of the above

Definitions and Diagnostic Criteria for Mixed Episodes in BD Have Broadened From DSM-IV to DSM-5.0

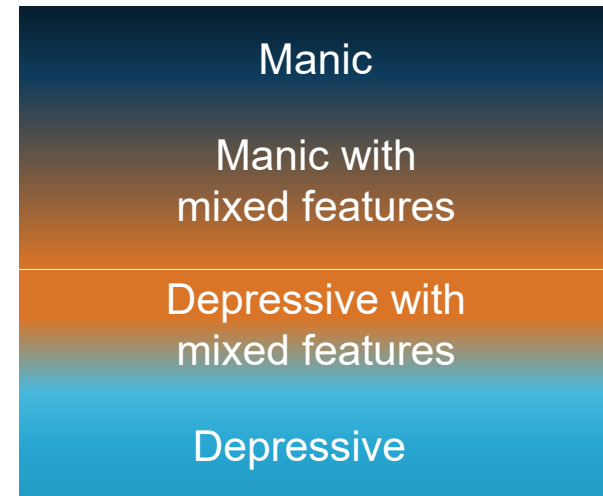
DSM-IV definition: mixed episode



Key points

Criteria met for both manic episode and major depressive episode nearly every day for ≥ 1 week^{1,2}

DSM-5.0 definition: episode with “mixed features”



Key points

Full criteria are met for syndrome episode and ≥ 3 non-overlapping symptoms of the opposite polarity are present¹⁻³

BD, bipolar disorder; DSM, Diagnostic and Statistical Manual of Mental Disorders.

1. Hu et al. *Prim Care Companion CNS Disord.* 2014;16:PCC.13r01599. 2. Fagiolini et al. *CNS Drugs.* 2015;29:725-740. 3. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. 2013.

Audience Polling Question

Now that mixed features can be applied to depressive, manic, or hypomanic states, I believe that more people will be diagnosed with mixed states. True or false?

A. True

B. False

Several Questions About Mixed States Remain



How should “mixed” states be defined?

What are the clinical implications of DSM-5.0 criteria?

What is the relationship between mixed states and substance abuse and suicidality comorbidities?

Why are mixed states more common in women?

What are effective treatment options?

DSM-5.0, Diagnostic and Statistical Manual of Mental Disorders, 5th edition.

Summary

In the DSM-5.0, the specifier “with mixed features” has broadened the definition and diagnostic criteria for mixed states in BD^{1,2}

Mixed states are common in BD and entail more challenging symptomatology than pure presentations²

Compared with patients with pure states, patients with mixed states have higher rates of substance abuse³ and suicidality⁴

Given the novelty of the DSM-5.0, data supporting treatment options for DSM-5.0 mixed states are limited

BD, bipolar disorder; DSM-5.0, Diagnostic and Statistical Manual of Mental Disorders, 5th edition.

1. Hu et al. *Prim Care Companion CNS Disord.* 2014;16:PCC.13r01599. 2. Fagiolini et al. *CNS Drugs.* 2015;29:725-740. 3. Tohen et al. *Harv Rev Psychiatry.* 1998;6:133-141. 4. Goldberg et al. *Am J Psychiatry.* 1998;155:1753-1755.

Questions



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